relating to $\bar{h}\,\bar{k}\,\bar{l}$ have been reflected about the real axis. We have from this diagram, since $\bar{F}_A'' = F_A''$ numerically,

$$F^2 = F'^2 + F_A''^2 + 2\,F'F_A'' \cos\theta$$

$$\bar{F}^2 = F'^2 + F_A''^2 - 2\,F'F_A'' \cos\theta$$

$$F'^2 = \tfrac{1}{2}(F^2 + \bar{F}^2) - F_A''^2$$

Thus

$$\Delta F^2 = (F^2 - \bar{F}^2) = 4\,F'F_A'' \cos\theta$$

and $$\cos\theta = \Delta F^2/4\,F'F_A'' \qquad (1)$$

If $F_A'' \ll F_A'$, an approximate formula is

$$\cos\theta = \Delta F/2F_A''. \qquad (2)$$

Here θ is the angle made by the non-anomalous part of the structure factor with the anomalous part. The phase of F' is obviously $\alpha = \pi/2 + \alpha_A - \theta$, if all the anomalous scatterers are of the same type, *e.g.*, all chlorines. If not, the phase angle ϕ between F_A'' and F_A' can be worked out from the known positions of the anomalous scatterers alone, and then

$$\alpha = \phi + \alpha_A - \theta$$

In the discussion below we shall confine ourselves to the former case when $\phi = \pi/2$ and the extension to the more general case is obvious.

Experimentally therefore, if the difference in intensity of the reflection *hkl* and its inverse $\bar{h}\,\bar{k}\,\bar{l}$ is measured accurately, then ΔF^2 can be calculated provided the scale factor is known. F_A'' can be calculated from the atomic co-ordinates of the anomalous scatterers (which can be obtained in most cases from a Patterson synthesis) and the known imaginary component of their atomic scattering factors and therefore θ can be obtained.

However, the solution for θ from cos θ is ambiguous, since θ can be either $+\theta$ or $-\theta$ and consequently the phase of F' determined in this way has the ambiguity given by

$$\alpha_{1,2} = \pi/2 + \alpha_A \pm \theta$$

This ambiguity is similar to the one occurring in the determination of phase by the isomorphous replacement method. In fact the scattering factor of the atoms A for the two reflections *hkl* and $\bar{h}\,\bar{k}\,\bar{l}$ are effectively different and this is made use of in the determination of phase.

Ambiguity and Its Resolution

If the group of anomalous scatterers is centrosymmetric, the phase angle α_A is 0 or π and in this case, the two possible values of the phase of F' are $\alpha_1 = \alpha$ and $\alpha_2 = \pi - \alpha$. It can be shown that if a Fourier synthesis is calculated using both the values of the phase, then the resulting diagram would contain, in addition to the peaks of the real structure, an equal number of negative peaks, at positions related to the former by an inversion about the inversion centre of the replaceable atoms. This diagram is similar to what one obtains by performing a Patterson synthesis with ΔF^2 which has been utilised by Pepinsky and collaborators for the determination of absolute configuration.[1] However it is superior to the latter in that only one duplication of the structure occurs and this too in the form of negative peaks, while in the ΔF^2 Patterson, a series of images of the structure as seen from each of the atoms in the set A occurs and the whole series is duplicated in the form of negative peaks about the inversion centre.

Experimental Verification

The method has been tested in the case of ephedrine hydrochloride[2] in which there are two chlorine atoms per unit cell. Only CuKα radiation was used and the anomalous dispersion of chlorine for this wavelength ($\Delta f'' = 0{\cdot}69$) was sufficient to give useful information. The difference in intensity between each pair of inverse reflections was measured accurately with a Geiger counter spectrometer for all the reflections of type *hk*0 and the phases were calculated from expression (2). The measurements were put on an absolute scale by using the reported values of F_C. The values of α as found by experiment are given in Table I together with the values of α calculated from the structure determined by conventional methods. The agreement is seen to be good, the differences rarely exceeding 20°.

Of the two possible values, the one which is nearer to the phase of the chlorine atoms may be chosen for a preliminary synthesis and thus the ambiguity resolved. This assumption is seen to be valid in nearly 75 per cent. of reflections as may be seen from Table I. The phases of those reflections for which the contribution from the chlorine atom is zero are indeterminate and this is a defect of the method. Such reflections are small in number and this difficulty is present even in the isomorphous replacement technique.

Combination of the New Method and Isomorphous Replacement Technique

An interesting possibility arises if a pair of isomorphous substances are available and the replaceable atoms are anomalous scatterers. This is possible for instance with hydrochlorides and hydrobromides